

Bone Mineral Density in Iranian Kidney Graft Recipients and Its Relation to Biochemical and PTH Serum Levels

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Abstract

Little is known about relation of transplantation and bone. We conducted a study to find out the frequency and predictors of osteoporosis in kidney transplanted patients in Iran. DEXA (DPX-MD, GE, Lunar corporation, USA) used for BMD of 61 kidney transplanted patients. Calcium, phosphate, alkaline phosphatase, BUN, creatinine and PTH, were also measured. Forty four percent of patients were men (27). Mean±SD of age of men and women was 44.3±10.44 and 40/7± 13.77, respectively. Mean±SD of transplant duration was 33.9± 33. 2 months Mean±SD of dialysis time was 12±14 months. 29.5% of patients had osteoporosis. Osteoporosis was significantly higher in subjects with BMI less than 19 kg/m² ($P= 0.007$). Alkaline phosphatase had a negative relation with osteoporosis in neck ($P= 0.001$). Other parameters had no significant relationship with osteoporosis. High prevalence of osteoporosis found in Iranian kidney graft recipients. Screening and therapeutic intervention in these patients is urgently needed.

Keywords: DXA, BMD, Osteoporosis, Kidney transplantation

Introduction

Patient survival following transplantation has improved significantly during the last decade, and long-term survival is now common. Attention has now been focused in preventing late complications and improving the patient's quality of life by trying to address factors that affect long term morbidity, including cardiovascular risk factors, immunosuppressive drug-induced renal dysfunction, and osteoporosis. Osteoporosis is characterized by low bone mass and architectural deterioration in bone tissue, which results in an increased susceptibility to fractures (1) and it is seen in high prevalence in patients who undergo renal transplantation (2, 3). It is specially prevalent in first 6 months af-

ter transplantation (4, 5, 6). Studies about risk factors of osteoporosis in these patients, considered Immunosuppressive drugs (7, 8), skeletal effects of ESRD and persistent hyperparathyroidism (that can be associated with abnormal level of calcium, phosphor and alkaline phosphatase) (9, 10) as risks of bone loss. Julian et al. (4) reported that this bone loss was isolated to the lumbar spine and was associated with low bone turnover, suggesting that it was secondary to the effects of glucocorticoids. Other studies have suggested that bone loss occurs at cortical sites as well (5, 6). However the consensus has been that the majority of bone loss occurs early after transplantation (when corticosteroid dosage is very high) and that the

rate of decline slows appreciably after 6-12 months (4, 5, 6). Data concerning the prevalence of osteoporosis after the first year of transplantation, are somewhat conflicting. Although some investigators have observed that bone loss is not progressive and that bone density returns to basal levels (11, 12) others have noted a persistently high rate of vertebral bone loss 8 or more years posttransplant (13, 14). However there is limited information about the prevalence of bone loss among renal graft recipients in south west region of Asia (specially who are in more than one year of transplantation. Therefore, we conducted a cross-sectional study for evaluation of bone status in Iranian renal transplanted patients, in different posttransplantation periods.

Materials and Methods

Subjects All patients were more than 2 months post renal transplantation and older than 20 y old. Patients with a prior history of Levothyroxine were excluded.

Study design The following baseline data were obtained about each subject: age, sex, weight, height, menopausal status, cause of renal failure, numbers of months on dialysis before transplantation, numbers of posttransplantation months, number of rejections, immunosuppression regimen employed and the cumulative dose of prednisolone and cyclosporine A. All subjects underwent bone mineral densitometry (BMD) at the hip (neck and total), and lumbar spine by dual-energy x-ray absorptiometry (DEXA) using a Lunar DPX-MD machine. Calcium, phosphate, alkaline phosphatase, BUN, creatinine and PTH also were measured.

As recommended by the World Health Organization (WHO), we defined patients in three diagnostic groups, Normal (T score above 1), osteopenia (T score between -1 and -2.5) and osteoporosis, (T score less than or equal to -2.5).

Statistical analysis Numerical results were presented as means \pm SD. Differences were con-

sidered significant at $P=0.05$. For analysis of relation between quantitative and qualitative parameters, multivariate qualitative parameters and quantitative parameters, and between qualitative parameters, we used logistic regression analysis, ANOVA, X² and Fisher's exact test, respectively. The SPSS 10 software was used for analysis of data.

Results

In this study, 44% of patients were men. The mean of age was 44.3 ± 10.44 and $40/7\pm 13.77$, respectively. Mean of transplant duration, dialysis time, cumulative prednisolone dose and cumulative cyclosporine A dose are shown in Table 1.

According to the World Health Organization definition, osteoporosis, was observed in 18 patients (29.5% of the total population) in any of the Total or Neck or L2-L4 regions (14.8% in Neck, 19.7% in total, 16.4% in L2-L4 regions). Rate of osteoporosis was significantly higher in who had BMI less than 19 kg/m² ($P=0.007$). Also Alkaline phosphatase had a negative relation with osteoporosis in neck region ($P=0.001$). Age, sex, transplantation duration, dialysis time, steroid and cyclosporine cumulative dosages, had no significant relationship with bone loss in any of regions. Also calcium, phosphate, BUN, creatinine and PTH had no relation with osteoporosis in different regions.

Frequency of different causes of renal failure among our patients is shown in Table-2.

Table 1: Patient demographic information and medical history

Parameters	
Men/women	27/34
Premenopausal/ postmenopausal women	11/34
Age of women (range)	40/7+- 13.77 (26-70)
Age of men (range)	44.3+- 10.44 (21-66)
BMI(range)	24.6+-5.2 (15.4-46.75)
dialysis time(range)	12+- 14 (0-72)
transplant duration (range)	33.9+- 33. 2 (3 - 172)
prednisolone cumulate dose (range)	12.68+-10.55 (2.83-6.84)
cyclosporine cumulative dose (range)	19.48+-17.51 (9-87)
Serum Ca level (range)	10.32±1.56 6-16
Serum P level (range)	3.34±0.70 2.1-6.1
Serum Alk Phos level (range)	213.47±119.95 85-702
Serum PTH level (range)	73.45±98.64 5-620s
Serum BUN level (range)	26.8±12.81 12-69
Serum Cr level (range)	1.16±0.27 0.7-2.36

Table2: Frequency of causes of renal failure

Causes of renal failure	frequency
Diabetes	4/61
Chronic lomerolunephritis	18/61
Hypertension	2/61
Polycystic disease	1/61
Congenital disease	1/61
Others	35/61

Discussion

In this study, osteoporosis prevalence in different regions of skeleton (neck and total region of femur and L2-L4 of spine) in 61 Iranian renal transplanted patients was evaluated and the effect of risk factors such as age, sex, BMI, menopausal status, cause of renal failure, duration of dialysis, duration of transplantation, number of rejections, the cumulative doses of prednisolone and cyclosporine A on it, was assessed.

There was no relationship between osteoporosis and age, sex and age of menopause in our patients. Which might be because of subjects' age, that in this period of life there is no significant difference in osteoporosis prevalence between ages and sexes. Also menopause is not common in these ages in women.

We found that duration of transplantation, dialysis time, cause of renal failure and history of rejection had no significant effect on the development of osteoporosis in the different regions. Our results also showed that high BMI had a beneficial effect on bone mass in lumbar region, findings that are in line with reports in the literature (12, 15)

It seems that a main mechanism contributing to bone loss in these patients, be use of immunosuppressive agents for prevention of rejection. But cumulative steroid exposure was not predictive of bone mass in our patients, a finding that concurs with some (11, 17) but not all of (4, 5, 16) previous reports. Also, cumulative cyclosporine exposure was not predictive of bone mass in our patients. It has been demonstrated to cause high-turnover bone loss in animal studies (7, 18), an effect that has been suggested (19, 20) but not yet proven to occur in humans. For explanation of our results and studies which are different with other researches that showed the significant effect of the above drugs in bone loss in renal transplanted patients (4), it has been suggested that the coadministration of cyclosporine and glucocorticoids may offset the individual effects of

each agent on bone turnover. Thus, in the initial posttransplant period, when doses of glucocorticoids are high, the steroid effect may be predominant, leading to a low bone turnover state. After the first year, maintenance glucocorticoid doses are low which may then “unmask” the high turnover state induced by cyclosporine (21).

Also Calcium, Phosphate, BUN, Creatinin and PTH had no relation with bone loss in these patients. As we know there is physiological relationship between calcium, phosphorus, Alk pho, PTH and bone mineral density and metabolism and changes in some of these parameters like calcium and PTH are established risk factors for osteoporosis (22-28). Finding no significant relationship between these parameters and bone loss may be due to adequate and suitable phosphate binder agents (calcium carbonate) and Vit D supplementation in ESRD patients (before transplantation) that is routine in Iranian ESRD patients. Another reason may be that our patients were in different periods after transplantation and disturbances in biochemical and hormonal levels is seen more in first months after transplantation. Also a study with larger sample size may show more significant relationship between them.

In summary, our results demonstrate that osteoporosis is common in Iranian renal transplant patients. Also posttransplantation osteoporosis is a complex disease with many factors play roles in its pathogenesis that some of them are unknown and some are; controversial, and more prospective studies with larger samples are needed for exact determination of them.

However, screening and therapeutic intervention for osteoporosis, in these patients, is urgently needed.

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